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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
LACOURCIERE,K	
ART UNIT	**PAPER NUMBER**
1635	6

DATE MAILED: 09/12/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

FILE

Office Action Summary

Application No.	Applicant(s)
09/383,894	LI
Examiner	**Group Art Unit**
Karen A. Lacourciere	1635

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-60* is/are pending in the applicat

Of the above, claim(s) *1-42 and 49-60* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *43-48* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences found in the specification have not been referred to using the appropriate SEQ ID NO. For example, Applicant is specifically directed to Figure 1, however, Applicant is urged to review the entire specification to be certain that all sequences therein are in compliance with 37 CFR 1.825(b).

A complete response to this Office action must comply with this request.

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-7, 20-24, and 29, drawn to a nucleic acid encoding a T-type calcium channel, classifiable in class 536, subclass 23.1.

II. Claims 8-13, drawn to an antisense molecule directed to a nucleic acid encoding a T-type calcium channel, classifiable in class 536, subclass 24.5.

III. Claims 14-19, drawn to a ribozyme directed at a nucleic acid encoding a T-type calcium channel, classifiable in class 536, subclass 23.2.

IV. Claims 25 and 26, drawn to a method of screening for a compound which effects a T-type calcium channel, classifiable in class 435, subclass 7.1.

V. Claims 27 and 28, drawn to a method of obtaining a DNA encoding a T-type calcium channel, classifiable in class 436, subclass 536.

VI. Claims 30-32, drawn to an oligomer which hybridizes to a nucleic acid encoding a T-type calcium channel, classifiable in class 536, subclass 24.3.

VII. Claims 33-36 and 40, drawn to a T-type calcium channel protein, classifiable in class 530, subclass 350.

VIII. Claims 37-39, 41 and 42, drawn to an antibody directed to a T-type calcium channel, classifiable in class 530, subclass 387.1.

IX. Claims 43-48, drawn to a method of modifying insulin secretion by pancreatic beta cells, classifiable in class 435, subclass 6.

X. Claims 49-55, drawn to a method of treatment for diabetes, classifiable in class 514, subclass 44.

XI. Claim 56, drawn to a method of modulating calcium levels, classifiable in class 514, subclass 2.

XII. Claim 57, drawn to a method of modulating the action potential of an L-type calcium channel, classifiable in class 514, subclass 2.

XIII. Claim 58, drawn to a method of modulating B-cell death, classifiable in class 514, subclass 2.

XIV. Claim 59, drawn to a method of modulating B-cell proliferation, classifiable in class 514, subclass 2.

XV. Claim 60, drawn to method of modulating calcium influx in an L-type calcium channel, classifiable in class 514, subclass 2.

1. The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and II are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, invention I has separate utility such as use for expression of a T-type calcium channel for purification. See MPEP § 806.05(d).

Inventions I and III are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, invention I has separate utility such as use for expression of a T-type calcium channel for purification. See MPEP § 806.05(d).

Inventions I and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group I can be used in a materially different method. For example, the nucleic acids of Group I can be used to over express a T-type calcium channel as part of a method of purification, which is materially different than the method of screening of Group IV.

Inventions I and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group I can be used in a materially different method. For example, the nucleic acids of Group I can be used to over express a T-type calcium channel as part of a method of purification, which is materially different than the method of obtaining DNA of Group V.

Inventions I and VI are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, invention I has separate utility such as use for expression of a T-type calcium channel for purification. See MPEP § 806.05(d).

Inventions I and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different products with different functions. The product of Group I is drawn to nucleic acids, which function to encode a protein and are composed of nucleotides, whereas the product of Group VII is drawn to a protein, which is composed of amino acids, and functions as a calcium channel.

Inventions I and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different products with different functions. The product of Group I is drawn to nucleic acids, which function to encode a protein and are composed of nucleotides, whereas the product of Group VIII is drawn to an antibody, which is composed of amino acids, and functions to bind to a protein.

Inventions I and IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group I can be used in a materially different method. For example, the nucleic acids of Group I can be used to over express a T-type calcium channel as part of a method of purification, which is materially different than the method of modifying insulin secretion of Group IX.

Inventions I and X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group I can be used in a materially different

method. For example, the nucleic acids of Group I can be used to over express a T-type calcium channel as part of a method of purification, which is materially different than the method of treatment for diabetes of Group X.

Inventions I and XI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group I can be used in a materially different method. For example, the nucleic acids of Group I can be used to over express a T-type calcium channel as part of a method of purification, which is materially different than the method of modulating calcium levels of Group XI.

Inventions I and XII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group I can be used in a materially different method. For example, the nucleic acids of Group I can be used to over express a T-type calcium channel as part of a method of purification, which is materially different than the method of modulating action potential of Group XII.

Inventions I and XIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group I can be used in a materially different method. For example, the nucleic acids of Group I can be used to over express a T-type calcium channel as part of a method of purification, which is materially different than the method of modulating B-cell death of Group XIII.

Inventions I and XIV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group I can be used in a materially different method. For example, the nucleic acids of Group I can be used to over express a T-type calcium channel as part of a method of purification, which is materially different than the method of method of modulating B-cell proliferation of Group XIV.

Inventions I and XV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP

§ 806.05(h)). In the instant case the nucleic acids of Group I can be used in a materially different method. For example, the nucleic acids of Group I can be used to over express a T-type calcium channel as part of a method of purification, which is materially different than the method of modulating calcium influx of Group XV.

Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to products which are materially different (ie. structurally) products which have different modes of operation. For example, the antisense molecules operate by binding to a nucleic acid, inhibiting the expression of said nucleic acid, whereas the ribozymes of Group III operate by catalyzing the cleavage of a nucleic acid.

Inventions II and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a product and a method of screening which have different functions and different effects. For example, the antisense of Group II functions to inhibit the expression of a nucleic acid, whereas the method of screening of Group IV functions to determine compounds which effect the action of a T-type calcium channel.

Inventions II and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different

functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a product and a method of screening which have different functions and different effects. For example, the antisense molecule of Group II functions to inhibit the expression of a nucleic acid, whereas the method of Group V functions to obtain a nucleic acid molecule.

Inventions II and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to products which have different functions and different effects. For example, the antisense molecule of Group II functions to inhibit the expression of a nucleic acid, whereas the oligomer of Group VI functions by hybridizing to and identifying a nucleic acid sequence.

Inventions II and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different products with different functions. The product of Group II is drawn to nucleic acids, which function to inhibit the expression of a nucleic acid and are composed of nucleotides, whereas the product of Group VII is drawn to a protein, which is composed of amino acids, and functions as a calcium channel.

Inventions II and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different products with different functions. The product of Group II is drawn to nucleic acids, which function to inhibit the expression of a nucleic acid and are composed of nucleotides, whereas the product of Group VIII is drawn to an antibody, which is composed of amino acids, and functions to bind to a protein.

Inventions II and IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group II can be used in a materially different method. For example, the nucleic acids of Group II can be used in an in vitro nucleic acid inhibition assay, which is materially different than the method of modifying insulin secretion of Group IX.

Inventions II and X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group II can be used in a materially different

method. For example, the nucleic acids of Group II can be used in an in vitro nucleic acid inhibition assay, which is materially different than the method of treatment for diabetes of Group X.

Inventions II and XI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group II can be used in a materially different method. For example, the nucleic acids of Group II can be used in an in vitro nucleic acid inhibition assay, which is materially different than the method of modulating calcium levels of Group XI.

Inventions II and XII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group II can be used in a materially different method. For example, the nucleic acids of Group II can be used in an in vitro nucleic acid inhibition assay, which is materially different than the method of modulating action potential of Group XII.

Inventions II and XIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group II can be used in a materially different method. For example, the nucleic acids of Group II can be used in an in vitro nucleic acid inhibition assay, which is materially different than the method of modulating B-cell death of Group XIII.

Inventions II and XIV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group II can be used in a materially different method. For example, the nucleic acids of Group II can be used in an in vitro nucleic acid inhibition assay, which is materially different than the method of method of modulating B-cell proliferation of Group XIV.

Inventions II and XV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP

§ 806.05(h)). In the instant case the nucleic acids of Group II can be used in a materially different method. For example, the nucleic acids of Group II can be used in an in vitro nucleic acid inhibition assay, which is materially different than the method of modulating calcium influx of Group XV.

Inventions III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a product and a method of screening which have different functions and different effects. For example, the ribozymes of Group III function to cleave a nucleic acid, whereas the method of screening of Group IV functions to determine compounds which effect the action of a T-type calcium channel.

Inventions III and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a product and a method of screening which have different functions and different effects. For example, the ribozymes of Group III function to cleave a nucleic acid, whereas the method of Group V functions to obtain a nucleic acid molecule.

Inventions III and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different

inventions are drawn to products which have different functions and different effects. For example, the ribozymes of Group III function to cleave a nucleic acid, whereas the oligomer of Group VI functions by hybridizing to and identifying a nucleic acid sequence.

Inventions III and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different products with different functions. The product of Group III is drawn to nucleic acids, which function to cleave a nucleic acid, and are composed of nucleotides, whereas the product of Group VII is drawn to a protein, which is composed of amino acids, and functions as a calcium channel.

Inventions III and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different products with different functions. The product of Group III is drawn to nucleic acids, which function to cleave a nucleic acid, and are composed of nucleotides, whereas the product of Group VIII is drawn to an antibody, which is composed of amino acids, and functions to bind to a protein.

Inventions III and IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product

as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group III can be used in a materially different method. For example, the nucleic acids of Group III can be used in an in vitro RNA cleavage reaction, which is materially different than the method of modifying insulin secretion of Group IX.

Inventions III and X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group III can be used in a materially different method. For example, the nucleic acids of Group III can be used in an in vitro RNA cleavage reaction, which is materially different than the method of treatment for diabetes of Group X.

Inventions III and XI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group III can be used in a materially different method. For example, the nucleic acids of Group III can be used in an in vitro RNA

cleavage reaction, which is materially different than the method of modulating calcium levels of Group XI.

Inventions III and XII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group III can be used in a materially different method. For example, the nucleic acids of Group III can be used in an in vitro RNA cleavage reaction, which is materially different than the method of modulating action potential of Group XII.

Inventions III and XIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group III can be used in a materially different method. For example, the nucleic acids of Group III can be used in an in vitro RNA cleavage reaction, which is materially different than the method of modulating B-cell death of Group XIII.

Inventions III and XIV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the

product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group III can be used in a materially different method. For example, the nucleic acids of Group III can be used in an in vitro RNA cleavage reaction, which is materially different than the method of method of modulating B-cell proliferation of Group XIV.

Inventions III and XV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group III can be used in a materially different method. For example, the nucleic acids of Group III can be used in an in vitro RNA cleavage reaction, which is materially different than the method of modulating calcium influx of Group XV.

Inventions IV and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different methods with different method effects. For example, the method of Group IV has the effect of determining a compound, which is materially different than the methods of Group V, which have the effect of obtaining a DNA molecule.

Inventions VI and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a product and a method of screening which have different functions and different effects. For example, the oligomers of Group VI function by hybridizing to and identifying a nucleic acid sequence, whereas the method of screening of Group IV functions to determine compounds which effect the action of a T-type calcium channel.

Inventions IV and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the protein of Group VII can be used in a materially different method, for example in a method of making an antibody.

Inventions IV and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody of Group VIII can be used in a materially different method, for example in an affinity purification step for obtaining a protein.

Inventions V and VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the oligomer of Group VI can be used as a primer in a PCR reaction.

Inventions V and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a product and a method which have different functions. For example, the method of Group V functions to obtain a DNA molecule, which is different than the protein of Group V, which functions as a T-type calcium channel.

Inventions V and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a product and a method which have different functions. For example, the method of Group V functions to obtain a DNA molecule, which is different than the antibody of Group V, which functions to bind to a protein.

Inventions VI and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different

functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different products with different functions. For example, the oligomer of Group VI is composed of nucleotides and functions by binding to a nucleic acid sequence, which is materially different than the protein of Group VII, which is composed of amino acids and functions as a T-type calcium channel.

Inventions VI and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different products with different functions. For example, the oligomer of Group VI is composed of nucleotides and functions by binding to a nucleic acid sequence, which is materially different than the antibody of Group VIII, which is composed of amino acids and functions to bind to a protein.

Inventions VII and VIII are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, invention VII has separate utility such as in a method of screening for T-type calcium inhibitors. See MPEP § 806.05(d).

Inventions IV and V and IX and X and XI and XII and XIII and XIV and XV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are draw to

methods which modulate activities of a T-type calcium channel, however, the methods of each of Groups IV and V and IX and X and XI and XII and XIII and XIV and XV differ materially in the particular method, the steps thereof, and modes of action/effects/operation to the extent that the scientific considerations of each Group makes each of the methods claimed therein to be distinct such that each Group would support its own patent. The fact that certain Groups recite and/or overlap in classification is merely an artifice of the classification schedule, and does not point to the fact that the search for each would be the same. Since the scientific considerations would be different for the methods for each of the above named Groups, a different search would necessarily be required for each, even though some of the Groups overlap or name the same classification.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Peter Regowski on January 27, 2000 a provisional election was made with traverse to prosecute the invention of Group IX, claims 43-48. After further consideration, it has been recognized that claim 49 should have been included in Group IX. Therefore, this Office action provides an examination of claims 43-49.

Claims 1-42 and 50-60 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Affirmation of this election must be made by applicant in replying to this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modifying beta cell insulin secretion using known calcium channel blockers, does not reasonably provide enablement for modifying beta cell insulin secretion using any calcium channel blocker or inhibitor of channel formation, ribozyme, antisense or an expressed gene *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Claims 43-49 are drawn broadly to methods of modulating insulin secretion in pancreatic beta cells by modifying levels of functional T-type calcium channels by any mechanism, including modulating insulin secretion *in vivo* (whole organism). Claims 43-46 are further drawn to modifying levels of functional T-type calcium channels using antisense or expressing a nucleic acid encoding a T-type calcium channel in any setting, including *in vivo* (whole organism).

The specification provides examples wherein T-type calcium channel blockers, including mibefradil and $NiCl_2$ are administered to pancreatic cells, *in vitro* (cell culture) and T-type calcium channel activity is blocked. There are no examples provided in the instant specification wherein an inhibitor of channel formation, an antisense molecule, a ribozyme or an expressed pancreatic T-type calcium channel are demonstrated to alter insulin secretion in beta cells in any setting, including *in vitro*. Further, there are no examples provided by the instant specification wherein an antisense molecule or a ribozyme are demonstrated to alter the level of a T-type calcium channel or alter the expression of a nucleic acid encoding a T-type calcium channel in any setting, including *in vitro*.

At the time the instant invention was made, modifying insulin secretion in beta cells in vivo (whole organism) via calcium channel blockers was unpredictable (see for example Verma, S. et al. page 126), calcium channel blockers reported to inhibit insulin secretion *in vitro* do not predictably produce the same effect *in vivo*. The reason for this variability was unknown, and one

skilled in the art would not be able to predict what calcium channel blockers would modify insulin secretion *in vivo* (whole organism), based on *in vitro* screening.

Further, the claimed methods read on *in vivo* (whole organism) methods of modifying insulin secretion using nucleic acid based drugs, including antisense, ribozymes and gene therapy methods. At the time the instant invention was made, and even now, *in vivo* (whole organism) methods using antisense, ribozymes and gene therapy were highly unpredictable (see, for example, Branch, Agrawal, Rossi, Anderson and Verma, I. et al.) due to issues including the determination of accessible target regions, how to specifically deliver an antisense molecule, ribozyme or gene therapy vector to a target cell at a concentration effective to result in a desired effect, and, in the case of gene therapy, the determination of target cell specific vectors and promoters to achieve and maintain expression of the gene.

The specification, as filed, provides only general guidance with regard to such factors. Due to the unpredictability in the art, the field to date does not have guidelines which would enable one skilled in the art to routinely practice methods drawn to *in vivo* applications of antisense, ribozymes and gene therapy. As such, one skilled in the art would need to determine such factors de novo, through empirical, undue trial and error experimentation. The skilled artisan would need to first determine what compounds interfere with T-type calcium channel pore formation and what ribozyme and antisense sequences are able to inhibit the expression of a nucleic acid encoding a pancreatic T-type calcium channel, *in vivo* or *in vitro*. Further, one skilled in the art would need to determine which of these compounds change the level of

functional t-type calcium channels in a manner and to the degree that insulin secretion would be modified. Additionally, one skilled in the art would need to determine how to deliver antisense molecules, ribozymes or gene therapy vectors specifically to pancreatic beta cells, in vivo, at a concentration which is effective to change the level of functional t-type calcium channels, and modify insulin secretion in said beta cells. This would include the determination of such factors as dosage, route of administration, disposition of the antisense molecule in tissues, and the half life and stability of the antisense or ribozyme molecule *in vivo*. For gene therapy, in particular, it would require the determination of an appropriate vector and enhancer-promoter combination for beta-cells "the search for such combinations is a case of trial and error for a given type of cell."(see Verma, for example p 240, columns 2 and 3) in order to get a high and sustained expression of a t-type calcium channel, such that beta cell insulin secretion would be modified.

Therefore, based on the breadth of the claims, the nature of the invention, the state of the art, the high level of unpredictability in the art, the lack of specific guidance by the inventor, the lack of working examples, and the quantity of experimentation that would be required, it would require undue experimentation, beyond what is taught in the specification, to practice the methods as claimed, over the full scope claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 43 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Verma, S. et al.

Verma, S. et al. disclose a method wherein hypertensive rats are administered mibefradil, a T-type calcium channel blocker, with a resultant decrease in insulin secretion, which would necessarily be a decrease in insulin secretion by the rat beta cells.

Therefore, Verma et al. anticipates claims 43 and 47.

Claims 43 and 47 are rejected under 35 U.S.C. 102(a) as being anticipated by Bhattacharjee et al.

Bhattacharjee et al. disclose a method wherein rat beta cells (INS-1) are contacted *in vitro* (cell culture) with $NiCl_2$, with a dose dependent reduction in glucose stimulated insulin secretion.

Therefore, Bhattacharjee et al. anticipates claims 43 and 47.

Claim 43 is rejected under 35 U.S.C. 102(b) as being anticipated by Kato et al.

Kato et al. disclose a method wherein neonatal rats are treated with streptozocin, increasing the level of functional T-type calcium channels, evidenced by the increased Ba^{2+} induced currents, and increasing insulin secretion.

Therefore Kato et al. anticipates claim 43.

Any inquiry concerning this communication should be directed to Karen A. Lacourciere at telephone number (703)308-7523.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott can be reached at (703) 308-4003. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Lacourciere
September 7, 2000

ANDREW WANG
PATENT EXAMINER
TC 1600